CLAIMS AMENDMENTS

Please amend the claims as follows:

Claims 1-28 (cancelled)

29. (currently amended) An isolated oligonucleotide specifically hybridizable under moderate stringency hybridization conditions, equivalent to 40% formamide with 5x or 6x SSC, wash conditions 2X SSC/ 0.1% SDS, to the nucleic acid molecule encoding on expression a soluble leptin receptor polypeptide selected from the group consisting of:

a. a DNA molecule of SEQ ID NO: 9; and

b. a DNA molecule that codes on expression for the soluble leptin receptor polypeptide encoded by ~~any of~~ the foregoing DNA molecules,

wherein said oligonucleotide does not hybridize under moderate stringency hybridization conditions to nucleic acid encoding the leptin receptor polypeptide of SEQ ID NO: 84.

30. (currently amended) An isolated oligonucleotide specifically hybridizable under moderate stringency hybridization conditions, equivalent to 40% formamide with 5x or 6x SSC, wash conditions 2X SSC/ 0.1% SDS, to the nucleic acid molecule which codes on expression for a soluble leptin receptor polypeptide selected from the group consisting of:

a. a soluble leptin receptor OB-Re (SEQ ID NO:10); and

b. a leptin receptor of amino acids 28-805 of SEQ ID NO:10,

wherein said oligonucleotide does not hybridize under moderate stringency hybridization conditions to nucleic acid encoding the leptin receptor polypeptide of SEQ ID NO: 84.

31. (currently amended) An isolated oligonucleotide specifically hybridizable under moderate stringency hybridization conditions, equivalent e to 40% formamide with 5x or 6x SSC, wash conditions 2X SSC/ 0.1% SDS, to the nucleic acid molecule having the nucleotide sequence corresponding or complementary to the DNA sequence set forth in SEQ ID NO: 9, wherein said oligonucleotide does not hybridize under moderate stringency hybridization conditions to nucleic acid encoding the leptin receptor polypeptide of SEQ ID NO: 84.

Claims 32- 66 (cancelled)

67. (withdrawn and currently amended) A method for diagnosing body weight abnormalities in a mammal comprising detecting splice variants of soluble leptin receptor OB-R in a patient sample comprising contacting a sample suspected of containing splice variants of soluble leptin receptor OB-R with an oligonucleotide specifically hybridizable under moderate stringency hybridization conditions, equivalent to 40% formamide with 5x or 6x SSC, wash conditions 2X SSC/ 0.1% SDS, to the nucleic acid molecule which codes on expression for a soluble leptin receptor polypeptide selected from the group consisting of:

a. a leptin receptor OB-Re (SEQ ID NO:10); and
b. a leptin receptor of amino acids 28-805 of SEQ ID NO:10,

wherein said oligonucleotide does not hybridize under moderate stringency hybridization conditions to nucleic acid encoding the leptin receptor polypeptide of SEQ ID NO: 84.

68. (withdrawn and currently amended) A method for diagnosing body weight abnormalities in a mammal comprising detecting splice variants of soluble leptin receptor OB-R in a patient sample comprising contacting a sample suspected of containing splice variants of soluble leptin receptor OB-R with an oligonucleotide specifically hybridizable under moderate stringency hybridization conditions, equivalent to 40% formamide with 5x or 6x SSC, wash conditions 2X SSC/ 0.1% SDS, to the nucleic acid molecule which

codes on expression for a polypeptide selected from the group consisting of SEQ ID NO: 10, or allelic variants thereof, wherein said oligonucleotide does not hybridize under moderate stringency hybridization conditions to nucleic acid encoding the leptin receptor polypeptide of SEQ ID NO: 84.

69. (withdrawn and currently amended) A method for measuring the expression of splice variants of soluble leptin receptor OB-R in a patient sample comprising contacting a sample suspected of containing splice variants of soluble leptin receptor OB-R with a oligonucleotide specifically hybridizable under moderate stringency hybridization conditions, equivalent to 40% formamide with 5x or 6x SSC, wash conditions 2X SSC/ 0.1% SDS, to the nucleic acid molecule which codes on expression for a polypeptide selected from the group consisting of:

a. a leptin receptor OB-Re (SEQ ID NO:10); and

b. a leptin receptor of amino acids 28-805 of SEQ ID NO:10,

wherein said oligonucleotide does not hybridize under moderate stringency hybridization conditions to nucleic acid encoding the leptin receptor polypeptide of SEQ ID NO: 84.

70. (withdrawn and currently amended) A method for measuring the expression of splice variants of soluble leptin receptor OB-R in a patient sample comprising contacting a sample suspected of containing splice variants of soluble leptin receptor OB-R with a oligonucleotide specifically hybridizable under moderate stringency hybridization conditions, equivalent to 40% formamide with 5x or 6x SSC, wash conditions 2X SSC/ 0.1% SDS, to the nucleic acid molecule which codes on expression for a polypeptide selected from the group consisting of SEQ ID NO: 10, wherein said oligonucleotide does not hybridize under moderate stringency hybridization conditions to nucleic acid encoding the leptin receptor polypeptide of SEQ ID NO: 84.

71. (withdrawn) The method of any of claims 67-70 wherein the oligonucleotide is labeled.

72. (withdrawn) The method of any of claims 67-70 wherein the nucleic acid molecule is RNA.

73. (withdrawn and currently amended) The method of any of claims 67-70 wherein the oligonucleotide is selected from the group consisting of ~~SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24,~~ SEQ ID NO:30~~,~~ and SEQ ID NO:31 ~~, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54~~.

74. (new) The isolated oligonucleotide of claim 29 wherein the oligonucleotide is selected from SEQ ID NO: 30 and SEQ ID NO:31.

REMARKS

The foregoing amendments and the following remarks are submitted in response to the communication dated February 23, 2006.

Status of the Claims

Claims 29-31 and 67-74 are pending in the application. Claims 29, 30 and 31 have been amended in order to more particularly point out and distinctly claim that which Applicants regard as the invention. Applicants have added new claim 74, directed to particular exemplary oligonucleotides. Applicants have amended withdrawn claims 67-70 and 73, which are withdrawn process claims, to include the limitations of the product claims. Support for the new and amended claims can be found generally through Applicants' specification.

Maintained Rejections

Claim Rejections – 35 U.S.C. §112

Claims 29-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The Examiner remarks that the claims are inadequate because they are drawn to an isolated oligonucleotide "specifically" hybridizable under moderate stringency conditions, equivalent to 40% formamide with 5X or 6X SSC. The Examiner remarks that part of the prior rejection has been overcome in the amendment to "equivalent". The Examiner remarks and asserts that there are no temperatures or wash conditions recited in the claims, which are important in defining the hybridization conditions and therefore which nucleic acid molecules would hybridize, and therefore the claims do not clearly set forth the metes and bounds of the patent protection desired. Applicants again submit that the specification provides a clear definition of hybridization conditions and assert that the skilled artisan can readily determine and use equivalent hybridization conditions. Applicants respectfully submit that the recitation of wash conditions is not required by the skilled artisan for him/her to determine or test equivalent hybridization conditions which will result in specific

hybridization of an isolated oligonucleotide to Ob-Re (as SEQ ID NO:9 nucleic acid, or other nucleic acid encoding OB-Re (SEQ ID NO:10)). The Specification, including at pages 37, 40 and 82, describes hybridization conditions for screening and amplification of specific OB-R forms. In particular, at page 40, lines 5-19, it is described that OB-R primers will amplify DNA under moderate to high stringency conditions, and the conditions are provided. The specific amplification of particular Ob-R forms is further detailed and exemplary OB-R specific primer pairs are set out in Example 1 in the Specification. In these sections, including at page 40 and 82, wash conditions are provided. For example, at page 40, lines 5-19, wash conditions of 2X SSC/ 0.1% SDS are described. In accordance with the Specification at page 40, lines 17-19,

> According to the invention, the above-noted PCR probes will define a nucleic acid molecule, *e.g.*, DNA, encoding OB-R from human as well as murine DNA libraries under similar hybridization conditions.

Thus, without question, similar or equivalent hybridization conditions are contemplated. Applicants have above amended the claims to provide for wash conditions in the claims. Applicants assert that the above arguments and amendments serve to obviate the maintained 35 U.S.C. § 112, second paragraph, rejections and request that they be withdrawn.

New Rejections or Objections

Claim Rejections - 35 U.S.C. §112

Claim 29 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The Examiner objects to the language "encoded by **any** of the foregoing DNA molecules", as there is only one foregoing DNA molecule. Applicants have above amended the language of claim 29 subpart b to recite "encoded by the foregoing DNA molecule".

Claims 29-31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The Examiner sets this out as a new matter rejection, asserting that there is no description in the Specification for conditions "equivalent to" in the recitation "moderate stringency hybridization conditions equivalent

to". Applicants respectfully disagree. Applicants again submit that the specification provides a clear definition of hybridization conditions and assert that the skilled artisan can readily determine and use equivalent hybridization conditions. The Specification, including at pages 37, 40 and 82, describes hybridization conditions for screening and amplification of specific OB-R forms. Page 37 describes "moderate stringency hybridization conditions correspond to a higher T_m, *e.g.*, 40% formamide, with 5x or 6x SSC". Thus, 40% formamide, with 5X or 6X SSC is one example of suitable moderate stringency conditions. At pages 40 and 82, equivalent conditions are set out, using the commercially available RAPID-HYB buffer (Amersham Life Sciences) for hybridization in moderate to high stringency conditions. In accordance with the Specification at page 40, lines 17-19,

> According to the invention, the above-noted PCR probes will define a nucleic acid molecule, *e.g.*, DNA, encoding OB-R from human as well as murine DNA libraries under similar hybridization conditions.

Thus, without question similar or equivalent hybridization conditions are contemplated and taught. Applicants assert that the claims comply with the written description requirement.

Claims 29-31 are further rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, stating that the specification has not described the subgenus of oligonucleotides that would bind to the DNA molecule of SEQ ID NO:9, but not the DNA encoding the polypeptide of SEQ ID NO:84. Applicants respectfully disagree and submit that the specification <u>does</u> describe oligonucleotides that bind to SEQ ID NO:9, but do not bind DNA encoding the polypeptide of SEQ ID NO:84 (the Tartaglia OB-R polypeptide sequence), including for example at pages 75-76, wherein specific RT PCR primers for OB-Re are provided. The specific amplification of particular OB-R forms is detailed and exemplary primer pairs are set out in Example 1 in the Specification. In Example 1, OB-Re specific primers, set out at pages 75-76, corresponding to SEQ ID NO: 30 and 31, were used in RT-PCR studies to specifically amplify the OB-Re form, as described:

> *Tissue distribution of the alternatively spliced leptin receptor.* RT-PCR was performed as described. The primer sequences for OB-Ra, OB-Rb, OB-Rc, and OB-Rd are shown above. The primers for OB-Re were: f 5′ TGTTATATCTGGTTATTGAATGG (SEQ ID NO:30), r 5′ CATTAAATGATTTATTATCAGAATTGC 3′ (SEQ ID NO:31).

The results of these RT-PCR studies for expression of the various OB-R forms are described at page 78-79, and depicted in Figure 6:

> The OB-Rb leptin receptor is expressed at a high level in the hypothalamus relative to other tissues (Figure 6). Lower level expression is seen in testes with an even lower level in adipose tissue. The other alternatively spliced mRNAs are expressed in several tissues including in some cases hypothalamus (Figure 6). OB-Re, which encodes a putative soluble receptor, is highly expressed in adipose tissue and is expressed at a lower level in brain, heart, and testes (Figure 6E).

Figure 6E depicts only a single band in each lane, i.e. only a single product of RT-PCR with primer pairs SEQ ID NO: 30 and 31. No other OB-R product (depicted as a different sized band on the gel) is shown in Figure 6E. This primer pair, which is directed to the unique C-terminal sequence of OB-Re, does not amplify the other forms including the OB-R form of Tartaglia. Applicants further point out and underscore that the sequence which is unique in OB-Re, specifically the amino acids after His^{796}, corresponding to GMCTVLFMD, as depicted in Figure 2 and provided in SEQ ID NO:120, are C-terminally encoded by the nucleotides of the nucleic acid encoding OB-Re (SEQ ID NO:9). The skilled artisan will readily recognize that these 9 C-terminal amino acids correspond to the last 27 nucleotides of SEQ ID NO:9, just before the termination 'tag' codon. The skilled artisan could, using the description and sequences disclosed in the specification and his/her own significant skill and knowledge, design further primers and primer pairs specific to OB-Re, including being directed to these unique nucleic acids.

In view of the foregoing remarks and amendments, Applicants submit that the Examiner's new rejections or objections under 35 U.S.C. § 112, second paragraph, may properly be withdrawn.